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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/999,690	09/08/1997	WALTER H. GUNZBURG	GSF97-03A	4218

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HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/999,690	Applicant(s) GUNZBURG ET AL.	
	Examiner Q. Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-23,25-28,30,31,34-40,42-49 and 52-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,9,11,12,16-21,23,25,27,28,30,34,35,37,38,42-47,49,52-57,59,60,62,63,66-71,73,74,76,77* is/are rejected.

7)☒ Claim(s) *5-7,10,13-15,22,26,31,36,39,40,48,58,61,64,65,72 and 75* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 30, 2002 has been entered.

The request for reconsideration filed on August 30, 2002 has been entered and assigned as Paper #24. Claims 3, 24, 29, 32, 33, 41, 50, and 51 have been canceled, claims 1, 2, 9, 12, 23, 27, 28, 30, 35, and 49 have been amended, claims 53-77 are newly submitted. Claims 1, 2, 4-23, 25-28, 30, 31, 34-40, 42-49, 52-77 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Objections

Claims 20, 21, 46, 47, 70, and 71 are objected to because of the following informalities: Each claim should begin with a capital letter, preferably an article such as "A", "The", etc. See MPEP § 608.01(m). Appropriate correction is required.

Claims 5-7, 10, 13-15, 22, 26, 31, 36, 39, 40, 48, 58, 61, 64, 65, 72, and 75 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION REQUIREMENT

The prior rejection of claims 1-52 has been modified and applies to amended and new claims 1, 2, 4, 8, 27, 28, 30, 34, 55-57, and 59.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

These claims are drawn to a recombinant vector comprising retroviral vector DNA elements necessary for infection and expression in target cells, and one or more sequences that encodes a peptide selected from the group consisting of therapeutic peptides, cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines, in addition to antimicrobial peptide melittin, cecropin, and magainin.

In view of the guidance provided, the specification only teaches antimicrobial peptides and is silent with regard to what kind of therapeutic peptides the claims are encompassing. An adequate written description of a peptide requires more than a mere statement that it is part of the invention; what is required is a description of the peptide itself. It is not sufficient to define peptide solely by its principal biological property, i.e. **therapeutic, cell cycle regulatory, and antiproliferation, etc.**, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any peptide with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all peptides that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Therefore, the specification fails to provide an adequate written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant

art that the inventors, at the time the application was filed, had possession of the claimed invention.

ENABLEMENT REQUIREMENT

The prior rejection of claims 1-52 has been modified and applies to amended and new claims 1, 2, 4, 8, 16-19, 23, 25, 27, 28, 30, 34, 42-45, 49, 52-57, 59, 66-69, 73, 74, 76, and 77. Particularly, the specification, while being enabling for making a recombinant vector comprising antimcrobial peptides melittin, cecropin, magainin and analogue thereof, does not reasonably provide enablement for making a recombinant vector comprising a combination of recited anti-microbial peptides and *any* and *all* therapeutic peptides; and the specification, while being enabling for anti-tumor or anti-viral activities *in vitro*, does not reasonably provide enablement for treating any and all diseases selected from the group consisting of a genetic defect, cancer, and viral infections. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As indicated *supra* in the written description section, the specification fails to provide an adequate description for the broad classes of therapeutic peptides encompassed by the claims, and the specification is silent regarding the combined effects of various peptides when used together. One cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan cannot envision the detailed structures of therapeutic peptides encompassed by these claims, nor envision the effects of the combination from the teaching of using antimicrobial peptide

alone, thus would not know how to use the invention without first carrying out undue experimentation to determine which of the peptides would have the recited function, and what would be the effect of such combination. Therefore, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed

With regard to claims drawn to therapeutic methods, applicants argue in paper #24 that the claims are not solely directed to gene therapy, that the invention provides for non-therapeutic methods for introducing homologous and/or heterologous nucleotide sequence into human or animals cells in vitro or in vivo; applicants further submitted exhibits to argue that the specification is enabling for gene therapy.

The arguments have been carefully considered, but found not persuasive for reasons of record and following.

The rejected claims under this provision are drawn to gene therapy methods in vivo, even though claims 16, 42, and 66 do not require a particular therapeutic use, the claims clearly or implicitly state the intended use of the method in light of the specification. As taught in the specification, the utility for introducing nucleotide sequences into a mammal is for providing therapeutic agents or correction of genetic defects, thus the claims implicitly indicate the intended use. Claims 19 and 45 recite "a pharmaceutical composition", which clearly indicates the intended use and is defined as a composition for therapeutic use, to prevent, alleviate, treat, or cure a disease within the animal to which the substance is administered, therefore, these claims will be

evaluated by the standard. Likewise, claim 52 recites "a non-human host cell infected with a viron", which encompass cells in an animal in vivo. As indicated in the previous Office action, the specification fails to provide sufficient support for the full scope of the claims because the specification fails to teach the therapeutic effect for treating viral infection *in vivo*, the specification fails to identify or teach any genetic disease that could be treated by the claimed vector, and the specification fails to deliver the vector *in vivo* to an established tumor directly or via any other route of administration. Thus, the specification fails to provide an enabling disclosure even showing that the cells in an animal were actually infected by the claimed vector. The delivery of ex vivo vector-transfected tumor cells in a nude mouse model does correlate with the tumor therapy in humans. Therefore, the skilled artisan intending to practice the invention has to first carry out undue experimentation as they are broadly claimed.

With regards to the exhibits 1-4 submitted, the references are not drawn to using retroviral vector encoding antimicrobial peptides for in vivo gene therapy, thus, could not be used as the support for enabling gene therapy aspect of the claims in view of the highly unpredictable nature of the gene therapy art.

For the reasons of record and those set forth above, the instant specification fails to meet the enablement requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 21, 35, 47, 60, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are vague and indefinite because claims 21, 47, and 71 recite "RNA of a vector according to " a previous claim drawn to a recombinant DNA vector, it is unclear what material the claims are encompassing, thus, the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 20, 21, 46, 47, 70, and 71 are rejected under 35 U.S.C. 102(e) as being anticipated by *Gilboa* (US 5,658,775).

These claims as written are broadly drawn to mRNA of any host cells and retroviral provirus produced by infection of target cells with a retroviral particle comprising a retroviral vector and a packaging cell line harboring at least one retroviral construct; and to any RNA including mRNA, rRNA and the total RNA of any retrovirus and the host cell.

Gilboa teaches a retroviral vector construct comprising a DNA sequence of interest (claim 1), wherein the DNA sequence will be transcribed into RNA under control of a promoter in the transfected host cells, wherein the RNA is a mRNA molecule (claim 12). Thus, *Gilboa* anticipates the instant claims.

Please note that amending claims 20, 21, 46, 47, 70, and 71 to recite the particulars of the recombinant vector in the base claims 1, 9, 35, and 60, respectively, could obviate this rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
November 18, 2002

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER